Attempted Kinetic Resolution of 1,2-Diols by Camphorquinone: Generation of (*R*)-(Chloromethyl)oxirane

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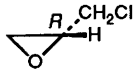
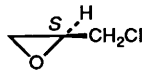
The epichlorohydrin (*R*)-(chloromethyl)oxirane has been prepared from *rac*-3-chloropropane-1,2-diol by means of the chiral ketone D-camphorquinone (1,7,7-trimethylbicyclo[2.2.1]heptane-2,3-dione). These reactions lead to intermediate dioxolanes which can be converted directly into oxiranes. This conversion was effected by reduction of the C-2-ketone of the dioxolane intermediate with sodium borohydride prior to reaction with hydrogen bromide–acetic acid followed by treatment of the resulting acetoxy bromide with sodium ethane-1,2-diolate. The diastereoselective formation of other dioxolanes was also investigated by reaction of D-camphorquinone with ethane-1,2-diol, propane-1,2-diol, and 3,3-dimethylbutane-1,2-diol.

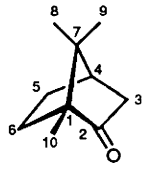
For studies into the toxicology of epoxides we required samples of (*R*)- and (*S*)-(chloromethyl)oxirane [epichlorohydrins (**1a**) and (**1b**), respectively]. These epoxides are also valuable precursors for the syntheses of several optically active compounds, especially certain drugs.[1] Although routes from D-mannitol to the oxiranes (**1a**) and (**1b**) have been described,[2] the syntheses are rather lengthy and two groups[3,4] have reported difficulties in achieving high optical purity.



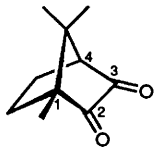
(**1a**)



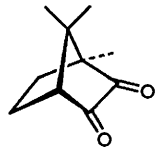
(**1b**)



(**3**)



(**2a**)



(**2b**)

A convenient route to optically active oxiranes developed by Golding *et al.*[5] uses the corresponding 1,2-diol as precursor. We have sought to prepare the oxirane (**1a**) [or (**1b**)] by kinetic resolution[6] of 3-chloropropane-1,2-diol using an optically pure chiral ketone to give an intermediate acetal that can be converted directly into the oxirane. Although there are many chiral ketones available we have used D-camphorquinone {1,7,7-trimethylbicyclo[2.2.1]heptane-2,3-dione, (**2a**)}. The use of (D)-camphor (**3**) was found to be less satisfactory.

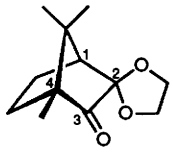
This paper describes in detail the reactions of a number of 1,2-diols with diketone (**2a**), and new routes to the optically pure enantiomers of chloromethyloxirane. Part of this work has been described in a preliminary communication.[7]

The reaction of a racemic 1,2-diol [$RCH(OH)CH_2OH$] with one enantiomer of a chiral ketone (R^1COR^2) will generate four diastereoisomeric dioxolanes, two from each enantiomer of the diol. The proportions of each diastereoisomer formed will be governed by the extent of interaction between R and R^1, and R and R^2, under conditions of both thermodynamic and kinetic control. Ideally, one diastereoisomer should predominate to permit its efficient separation, preferably by direct crystallisation from the mixture.

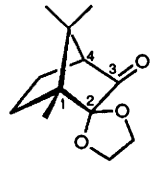
Casanova and Corey[8] separated the two diastereoisomers from the reaction of *rac*-camphor with D-(−)-butane-2,3-diol by GLC, enabling them to attain the resolution of camphor. Reaction of a number of chiral ketones with (*R*,*R*)-butane-2,3-diol gave diastereoisomeric mixtures from which enantiomeric purities of the starting ketones were determined by ^{13}C NMR spectroscopy.[9] Conversely the enantiomeric purities of 1,2-diols were measured by ^{13}C NMR and HPLC analyses of the diastereoisomeric products obtained in reactions of the diols with 2-substituted cyclohexanones.[10] No enantioselectivity was observed in the reaction of (*S*)-2-propylcyclohexanone with *rac*-propane-1,2-diol or other with 1,2-diols.

Results and Discussion

Reaction of 1,2-*Diols with* D-*Camphorquinone.*—(i) *Ethane-1,2-diol.* It was important to demonstrate that reaction of a 1,2-diol with diketone (**2a**) is regioselective for the less hindered carbonyl group (C-3) and that monoketal formation is much faster than diketal formation. Indeed, acid-catalysed reaction of D-camphorquinone (**2a**) with ethane-1,2-diol has been shown[11] to give principally the dioxolane (**4a**). We found that D-camphorquinone when heated for 18 h with ethane-1,2-diol in benzene at reflux containing a catalytic quantity of toluene-*p*-sulphonic acid (PTSA) gave a 6:1:4 mixture of (**4a**) derived from reaction at the 3-carbonyl group, the isomeric ketal (**4b**) from reaction at the 2-carbonyl group and the diketal from reaction at both carbonyl groups according to analysis by NMR. The ^1H NMR spectra of these ketals show a useful distinguishing feature. In the diketal 4-H appears at δ 1.68, whilst the corresponding resonance in compound (**4a**) is at δ 1.95 due to a deshielding effect of the carbonyl group. In the ketal (**4b**) 4-H resonates at δ 2.17 because of the greater deshielding effect of its carbonyl.

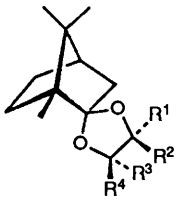


(**4a**)



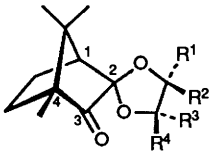
(**4b**)

(ii) *Propane-1,2-diol.* Reactions of either (*R*)- or (*S*)-propane-1,2-diol with D-camphor (**3**) in refluxing benzene or toluene containing a catalytic quantity of PTSA gave *ca.* 1:1 mixtures of the diastereoisomeric dioxolanes (**5a**) and (**5b**), and (**5c**) and

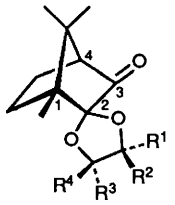


(5) a; $R^1 = R^2 = R^3 = H$, $R^4 = Me$
b; $R^1 = Me$, $R^2 = R^3 = R^4 = H$
c; $R^1 = R^3 = R^4 = H$, $R^2 = Me$
d; $R^1 = R^2 = R^4 = H$, $R^3 = Me$

(**5d**), respectively. However, the acid-catalysed reaction of (*S*)-propane-1,2-diol with D-camphorquinone (**2a**) in refluxing benzene for 20 h gave a 6:1 mixture of diastereoisomeric dioxolanes (**6a**) and (**6b**), respectively. Separation of these was achieved by column chromatography followed by recrystallisation to afford the predominant dioxolane (**6a**). When this dioxolane was heated in toluene containing a catalytic amount of PTSA (105 °C/96 h) it yielded a mixture of isomers (**6a**) and (**6b**) in the ratio 2:3. This suggests that the dioxolanes produced in refluxing benzene (84 °C) are products of kinetic control, whereas the ratio in toluene (105 °C) is a result of thermodynamic control.



(6) a; $R^1 = R^3 = R^4 = H$, $R^2 = Me$
b; $R^1 = R^2 = R^4 = H$, $R^3 = Me$
c; $R^1 = Me$, $R^2 = R^3 = R^4 = H$
d; $R^1 = R^2 = R^3 = H$, $R^4 = Me$



(6) e; $R^1 = R^2 = R^3 = H$, $R^4 = Me$

(7) a; $R^1 = R^2 = R^3 = H$, $R^4 = CH_2Cl$
b; $R^1 = R^3 = R^4 = H$, $R^2 = CH_2Cl$
c; $R^1 = CH_2Cl$, $R^2 = R^3 = R^4 = H$
d; $R^1 = R^2 = R^4 = H$, $R^3 = CH_2Cl$

(7) e; $R^1 = R^2 = R^3 = H$, $R^4 = CH_2Cl$
f; $R^1 = R^3 = R^4 = H$, $R^2 = CH_2Cl$
g; $R^1 = CH_2Cl$, $R^2 = R^3 = R^4 = H$
h; $R^1 = R^2 = R^4 = H$, $R^3 = CH_2Cl$

(8) a; $R^1 = R^3 = R^4 = H$, $R^2 = Bu^t$
b; $R^1 = R^2 = R^4 = H$, $R^3 = Bu^t$
c; $R^1 = Bu^t$, $R^2 = R^3 = R^4 = H$
d; $R^1 = R^2 = R^3 = H$, $R^4 = Bu^t$

The acid-catalysed reaction of (*R*)-propane-1,2-diol with D-camphorquinone (**2a**) in refluxing benzene gave a 6:5 mixture of dioxolanes (**6c**) and (**6d**). These were accompanied by isomeric ketals, one of which (**6e**) was fully characterised (see Experimental section). The total quantity of these ketals, which were formed in similar quantity to one another, was *ca.* $\frac{1}{7}$th of (**6c**) + (**6d**).

(iii) 3-*Chloropropane*-1,2-*diol*. We reported that an excess of *rac*-3-chloropropane-1,2-diol (10 mol equiv.) reacts with D-camphorquinone (**2a**) in refluxing benzene containing a catalytic quantity of PTSA to give a kinetically controlled mixture of the diastereoisomers (**7a–d**) in yields of 27, 45, 17, and 12%, respectively, determined by HPLC. In a subsequent investigation of this system using a superior method of HPLC analysis we found that actually eight compounds are formed and that these are all the possible monoketals. The true yields of (**7a–d**) are 23, 24, 14, and 14% and these are accompanied by the isomeric ketals (**7e–h**) (yields 7, 3, 5, and 10%, respectively—see Fig. 1). In the preliminary study the yield of (**7b**) was

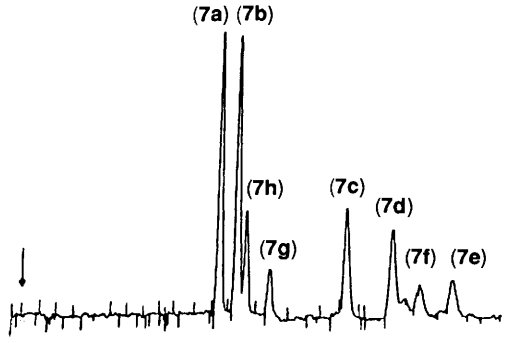


Fig. 1 HPLC separation of dioxolanes (**7a–h**)

overestimated because its HPLC peak was enhanced by two of the minor ketals. The major diastereoisomer (**7b**) could be separated by repeated fractional crystallisation from light petroleum, whilst the other isomers were separated by preparative HPLC. The resulting crystalline compounds were stable for long periods at 0 °C. As with compounds (**4a**) and (**4b**), the ketals from reaction of 3-chloropropane-1,2-diol with the 3-carbonyl of camphorquinone could be distinguished from the ketals from reaction at the 2-carbonyl by the position of 1-H/4-H (relatively deshielded in the ketals from reaction at the 2-carbonyl). For the assignment of structures the relative shielding or deshielding of the protons in the CH_2Cl group was also helpful. The spectra of the pairs (**7a**) and (**7h**), (**7b**) and (**7g**), (**7c**) and (**7f**), and (**7d**) and (**7e**) were all similar to one another because of the *pseudo* enantiomeric relationship of the members of each pair (they would be enantiomers but for the methyl group). This also explains why the ketals from reaction at the 2-carbonyl of camphorquinone were not observed in our initial study! The reaction of L-camphorquinone (**2b**) with an excess of *rac*-3-chloropropane-1,2-diol (10 mol equiv.) gave a crystalline product which is the enantiomer (**9**) of the dioxolane (**7b**).

When the dioxolane (**7b**) was heated in toluene (103 °C/96 h) containing a catalytic amount of PTSA it equilibrated with the dioxolane (**7d**) [ratio 1:1 at equilibrium as determined by ^1H NMR spectroscopy and HPLC]. Thus, dioxolanes (**7b**) and (**7d**) have the same chirality at the carbon atom bearing the chloromethyl group.

Reduction of compound (**7b**) with sodium borohydride to give the alcohols (**10a**) and (**10b**), [ratio 3:1, ^1H NMR], followed by treatment with 2M-HCl in methanol (3 h at reflux) gave 3-chloropropane-1,2-diol [55%, based on initial amount of the dioxolane (**7b**)]. Attempted direct hydrolysis of the dioxolane (**7b**) with 2M-HCl in methanol showed little reaction after 6 h at 80 °C. This resistance to hydrolysis probably derives from the destabilisation of the intermediate carbocation (**7e**) by the adjacent carbonyl (C-2) [*cf.* Scheme 1: hydrolysis is the reverse of the process shown].

The 3-chloropropane-1,2-diol obtained from the alcohols (**10a**) and (**10b**) was found to be chemically and optically pure by ^1H NMR spectroscopy (only one enantiomer was detected by the chiral shift reagent Eu(hfbc)$_3$,* and showed $[\alpha]_D^{19} -7.4°$ [lit.,[12] $[\alpha]_D^{20} +7.3°$ for the (*S*)-isomer]. This shows that the carbon bearing the chloromethyl group in isomers (**7b**) and (**7d**) possesses the (*R*)-configuration, whereas the dioxolane (**9**) must possess the (*S*)-configuration at this centre.

The structural assignments made for dioxolanes (**7a–h**) are additionally based on analysis of their 400 MHz ^1H NMR spectra, the chemical shifts of the dioxolane protons being exceptionally informative (Fig. 2). To confirm that compound (**7b**) has the chloromethyl *syn* to the carbonyl, we

* Europium trisheptafluorobutyrylcamphorate.

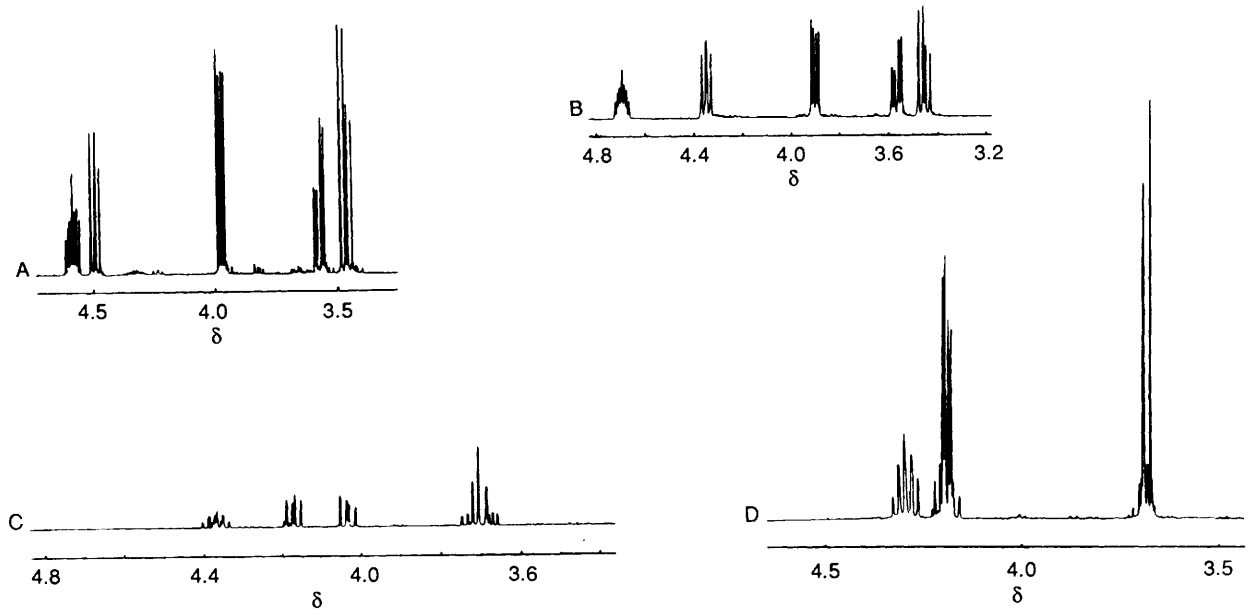
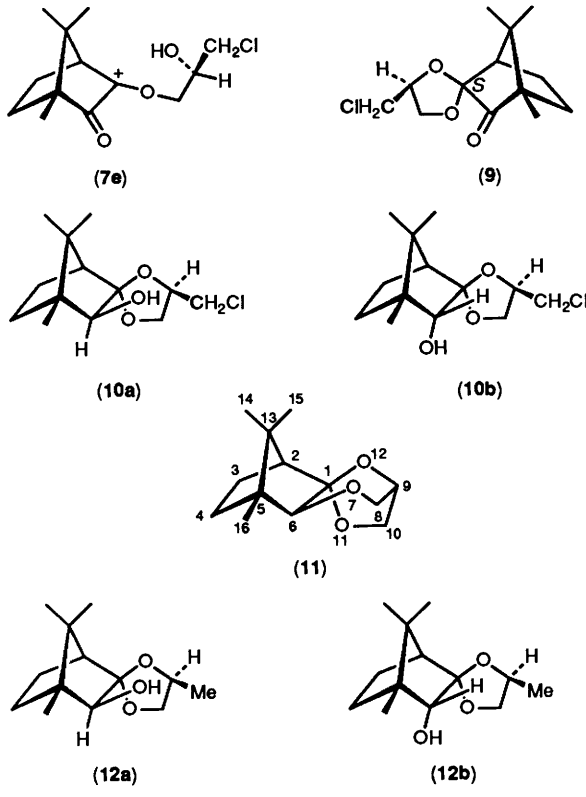


Fig. 2 400 MHz ^{1}H NMR spectra of the dioxolane moiety of: compound (**7d**), (**7c**), (**7b**), and (**7a**)

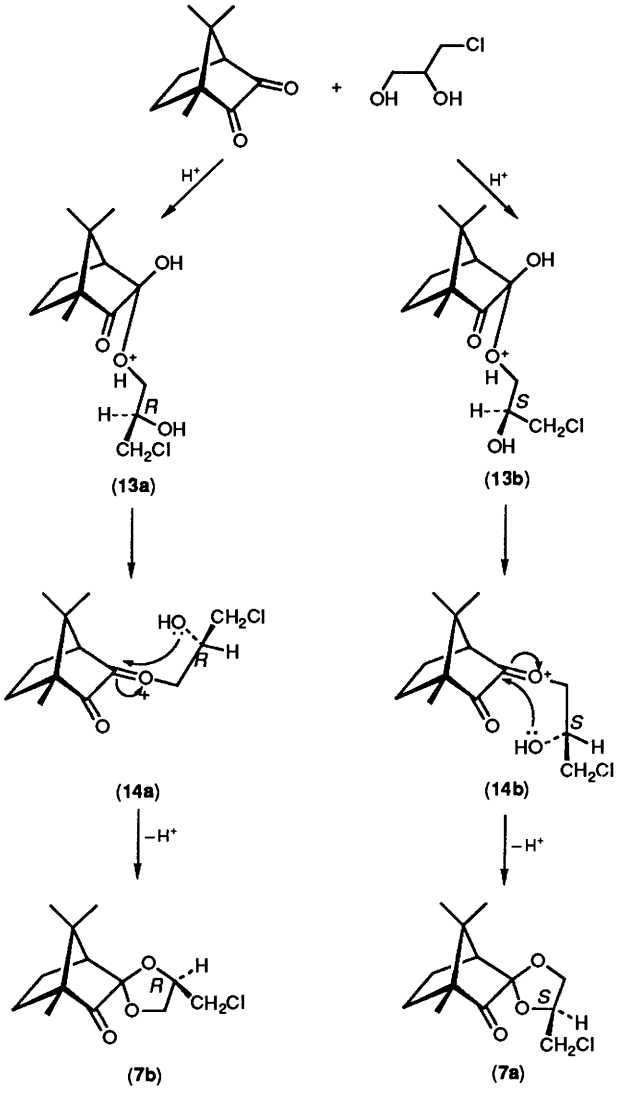


carried out diastereoselective reduction of the carbonyl group to give *exo*-alcohol (**10a**), followed by intramolecular S_N2 substitution to afford the dioxolane (**11**). For the reduction we initially explored the use of borane reagents but, even with diborane reduction was extremely slow. With lithium trimethoxyaluminium hydride, diastereoselective reduction of the carbonyl group to *exo*-alcohol occurred, but with concomitant reduction of the chloro function. The product mixture consisted of a 5:2 ratio of compounds (**12a**) and (**10a**). Excellent results were obtained by reduction with lithium tri-t-butoxyaluminium hydride, which gave a 96% yield of alcohol (**10a**). Treatment of this compound with sodium hydride in tetrahydrofuran (THF) gave the dioxolane (**11**). An interesting feature of the ^{1}H NMR spectrum of compound (**11**) is the additional 1 Hz coupling shown by resonances at δ 3.86 and 4.2. This results from a long-range interaction between exocyclic protons at C-8 and C-10.

It is necessary to show that the stereochemistries of the crystalline dioxolanes [(**6a**) and (**7b**), respectively] obtained from the reactions of (*S*)-propane-1,2-diol and *rac*-3-chloropropane-1,2-diol with D-camphorquinone (**2a**) are identical. Reduction of the dioxolane (**7b**) with L-Selectride [lithium tri-s-butylborohydride] (14 h/40 °C) gave the dioxolane (**12a**). The 300 MHz ^{1}H NMR spectrum showed no signals for the dioxolane (**12b**). Oxidation of compound (**12a**) with pyridinium dichromate (PDC) in dimethylformamide (DMF)[13] gave a single compound with properties identical with those of the dioxolane (**6a**).

(iv) 3,3-*Dimethylbutane*-1,2-*diol*. Increasing the bulk of the R group in $RCH(OH)CH_2OH$ should increase the steric interaction between R and R^1, and R and R^2, in the acetals formed from a chiral ketone R^1COR^2, and hence alter their ratio. This was confirmed by acid-catalysed reaction of *rac*-3,3-dimethylbutane-1,2-diol with D-camphorquinone (**2a**), which gave seven observed monoketals (HPLC analysis) from which the two major isomers were separated in yields of 60 and 15%. On the basis of their ^{1}H NMR spectra (comparison with data for the above ketals) both compounds are ketals derived from reaction at the 3-carbonyl of camphorquinone, but it is not possible to assign their structures with certainty.

Mechanism of Formation of the Dioxolane (**7b**).—The formation of the dioxolane (**7b**) presumably involves initial *endo*-attack of the primary alcohol of (*R*)-chloropropane-1,2-diol on C-3 of camphorquinone to generate the hemiacetal (**13a**) (see Scheme 1). The reaction with (*S*)-chloropropane-1,2-diol is presumably initiated by attack to give hemiacetal (**13b**). The hemiacetals then lose water to give the oxonium species (**14a**) and (**14b**), respectively. The predominant dioxolane (**7b**) is then formed from compound (**14a**) by *exo*-attack at C-3 by the secondary hydroxy group. This could be preferred over *endo*-attack leading to the isomeric dioxolane (**7d**) by analogy with preferred *exo*-capture of the norbornyl cation.[14] However, this is an oversimplification because the second most abundant dioxolane (**7a**) must form from compound (**14b**) by *endo*-attack at C-3 of the secondary hydroxy group, whilst *exo*-attack affords the dioxolane (**7c**). The most remarkable result of this study is the preference observed with propane-1,2-

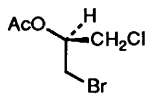


Scheme 1

diol and 3-chloropropane-1,2-diol for the kinetic formation of ketals from reaction at the 3-carbonyl of camphorquinone in which the dioxolane substituent is *syn* to the remaining carbonyl group. *Only* with the t-butyl substituent was kinetic resolution of the starting 1,2-diol observed, but further work is needed to confirm that the major ketal is the *syn*-isomer (**8b**).

Synthesis of (R)-(*Chloromethyl*)*oxirane* [(R)-*Epichlorohydrin*].—Golding *et al.*[5] have shown that the reaction of a 1,2-diol with 45% HBr in acetic acid (HBA) generates a vicinal acetoxy bromide, which on treatment with base cyclises to an oxirane. Our strategy was to treat the dioxolane (**7b**) directly with HBA and convert the intermediate vicinal acetoxy bromide into (*R*)-chloromethyloxirane (**1a**) by base-induced cyclisation.

Treatment of the dioxolane (**7b**) with HBA (60 °C/5 h) gave a mixture of products containing camphorquinone (**2a**) and (*S*)-2-acetoxy-1-bromo-3-chloropropane (**15**) [its chirality being inferred from the chirality of the dioxolane (**7b**) and the product oxirane]. It was later found that a much faster and milder reaction (25 °C/2.5 h) could be performed by reduction of the C-3 ketone of the dioxolane (**7b**) prior to HBA treatment. Attempts to purify the acetoxy bromide (**15**) by either fractional distillation or flash chromatography on silica were only partially successful and therefore the epoxide was obtained directly from the crude acetoxy bromide.



(15)

Thus, the product mixture from the reaction of the dioxolane (**7b**) with HBA was treated with sodium ethane-1,2-diolate in ethane-1,2-diol (1 mol equiv. $NaOCH_2CH_2OH$) and gave (*R*)-chloromethyloxirane (**1a**), which was distilled directly from the reaction mixture. The specific rotation of this material $[\alpha]_D^{24} - 33°$, was comparable to the highest literature values[2] [−34.3° for (*R*)-isomer, +33° for (*S*)-isomer]. ^{1}H NMR analysis of the product showed only one enantiomer on use of the chiral shift reagent Eu(hfbc)$_3$.

The method described is convenient for the preparation of optically active oxiranes from readily available racemic diols, when alternative methods (*e.g.*, Sharpless epoxidation,[15] derivation from the 'chiral pool'[16]) are not directly applicable.

Experimental

Materials and Instruments.—Solvents used in HPLC analyses were of HPLC grade and were purchased from Rathburn Chemicals Ltd., Walkerburn, Scotland. Other solvents were of AnalaR or laboratory grade. Where solvent purification or drying was necessary, solvents were purified by standard procedures.[17,18] All chemicals were of the highest purity commercially available and where necessary were purified prior to use.[18] TLC was performed on aluminium-backed Kieselgel 60 F_{254} plates (Merck Cat. No. 5554) 0.2 mm in thickness. CHN Combustion analyses were performed by C.H.N. Laboratories, Leicester; Shell Research Ltd., Sittingbourne, Kent; or The University of Newcastle upon Tyne. HPLC analyses were performed on a Waters or Gilson instrument. IR spectra were recorded on a Perkin-Elmer (model 580B) grating spectrophotometer. Samples were either mulls (medicinal white oil), films, or solutions and were run on or between NaCl plates. Mass spectra (CI and EI) were recorded on a Kratos MS80 spectrometer. FAB mass spectra were recorded on a V.G. 7070 mass spectrometer. M.p.s were determined using a Kofler block or an Electrothermal apparatus and are uncorrected. ^{1}H NMR spectra were recorded on one of the following instruments: a Bruker (WH-400) 400 MHz, (WH-360) 360 MHz, (WH-300) 300 MHz, GE QE-300 (300 MHz) or Perkin-Elmer (R34) 220 MHz. Tetramethylsilane was used as the internal standard in organic solvents, and 3-(trimethylsilyl)tetradeuteriopropionic acid sodium salt in D_2O (δ 0). ^{13}C NMR spectra were recorded on one of the following instruments: Bruker (WH-400) 100.62 MHz, (model WH-360) 90.52 MHz, or (WH-90) 22.63 MHz spectrometers. All spectra were run with broad-band ^{1}H decoupling. Optical rotations were recorded with a Bendix NPL automatic polarimeter (model 143D). The instrument was calibrated against a standard sucrose solution prior to each measurement. UV spectra were recorded with a Pye-Unicam (model SP-180) ultraviolet spectrophotometer. Except where noted otherwise, light petroleum refers to the fraction boiling in the range 60–80 °C.

Analysis of Product Mixtures.—For HPLC conditions see below. The diastereoisomeric ratios in the reactions of camphor (**3**) and camphorquinone (**2a**) with (*R*)- and (*S*)-propane-1,2-diol were also measured by ^{1}H NMR spectroscopy. All mixtures were analysed as solutions in $CDCl_3$ (with $SiMe_4$ as the internal standard) at concentrations of *ca.* 20 mg cm^{-3}. Dioxolanes (**5c**) and (**5d**) were analysed by integration of the methyl singlets at δ 0.99 and 1.0, and dioxolanes (**5a**) and (**5b**) by integration of the

diastereotopic methylene protons at δ 3.33 and 3.90 (one diastereotopic pair) and δ 3.51 and 4.02 (the other diastereotopic pair). Dioxolanes (**6a**), (**6b**), (**6c**) and (**6d**) were analysed by integration of their methyl doublets at δ 1.18 and 1.25 [for (**6c**) and (**6d**), respectively] and 1.28 and 1.34 [for (**6b**) and (**6a**)].

Preparation of D-*Camphorquinone* (**2a**).—Selenium dioxide (300 g, 2.97 mol) was added to a stirred solution of D-camphor (250 g, 1.64 mol) in acetic anhydride (250 cm^3) and the resulting suspension was then boiled under reflux for 24 h. A colour change from red-purple to green-grey occurred. After cooling, the suspension was filtered and washed with glacial acetic acid (*ca.* 200 cm^3). Camphorquinone was precipitated by careful neutralisation of the orange filtrate with 12M-potassium hydroxide (*ca.* 500 cm^3). The camphorquinone was filtered off, washed with water, dried (vacuum), and recrystallised to afford yellow needles (from light petroleum) (228.7 g, 84%), m.p. 195–196 °C [lit.,[19] 198 °C]; $\delta_H(CDCl_3)$ 0.94 (s, 3 H, Me), 1.07 (s, 3 H, Me), 1.11 (s, 3 H, Me), 1.65 (m, 2 H, 5-H_{exo} and 6-H_{exo}), 1.95 (m, 1 H, 5-H_{endo} or 6-H_{endo}), 2.19 (m, 1 H, 6-H_{endo} or 5-H_{endo}), and 2.65 (d, 1 H, CH); $\delta_C(CDCl_3)$ 8.59 (CH_3), 17.27 (CH_3), 20.91 (CH_3), 22.13 (CH_2), 29.84 (CH_2), 42.44 (C-7), 57.89 (CH), 58.54 (C-1), 202.67 (CO), and 204.7 (CO); ν_{max}(Nujol mull) 2 925s, 2 855s, 1 760s, 1 395s, 1 324m, 1 200m, 1 107m, 1 052m, 737m, and 696 cm^{-1}; *m/z* (EI) 166 (M^+), 138 $(M - CO)^+$, 110 $(M - 2CO)^+$, and 95 $(C_7H_{11}^+)$; $[\alpha]_D^{20}$ + 106.2° (*c* 1.0 in toluene).

Preparation of L-*Camphorquinone* (**2b**)—This was prepared from L-camphor (5 g, 3.28 × 10^{-2} mol) and selenium dioxide (6 g, 6 × 10^{-2} mol) in the manner described for D-camphorquinone, to give the L-quinone (**2b**) as yellow needles (3.93 g, 72%), m.p. 194–196 °C [lit.,[19] 198 °C]; $[\alpha]_D^{20}$ −108.4° (*c* 1.0 in toluene) {lit.,[19] $[\alpha]_D^{20}$ −109.8° (*c* 1.0 in toluene)}; all other physical properties were identical with those shown by D-camphorquinone (**2a**).

Preparation of (1S,4R)-4,7,7-*Trimethylbicyclo*[2.2.1]*heptane*-2-*spiro*-2′-(1′,3′-*dioxolan*)-3-*one* (**4**).—A stirred solution of D-camphorquinone (1 g, 6.02 mmol), ethane-1,2-diol (0.55 g, 8.8 mmol), and PTSA (0.1 g, 0.52 mmol) was heated at reflux in benzene (25 cm^3) under nitrogen for 24 h, in an apparatus which allowed the benzene condensate to percolate through a Soxhlet thimble containing dry magnesium sulphate. After cooling of the resulting solution, anhydrous sodium carbonate (0.5 g) was added to neutralise the acid. The solid was then filtered off and the solvent was removed at reduced pressure (rotary evaporator) to give a yellow oil. ^1H NMR analysis showed this to be a 6:1:4 mixture of the dioxolane (**4a**), its isomer (**4b**) and the 2,3-diketal. The oil was dissolved in diethyl ether (10 cm^3) and unchanged quinone was removed by repeated shaking with 40% aq. sodium hydrogen sulphite until the ether layer became very pale yellow. The ether layer was dried (sodium sulphate) and evaporated to give a white solid. Recrystallisation from light petroleum gave the spiro compound (**4**) as needles (0.66 g, 52%), m.p. 80–82 °C [lit.,[11] 81–83 °C]; $\delta_H(CDCl_3)$ 0.89 (s, 3 H, Me), 0.97 (s, 3 H, Me), 1.00 (s, 3 H, Me), 1.45–2.08 (m, 5 H, 1-H, 5-H_2, and 6-H_2), 3.97 (m, 2 H, *exo*-OCH_4CH_4O), and 4.21 (m, 2 H, *endo*-OCH_4CH_4O-); ν_{max}(hexachloro-1,3-butadiene mull) 2 960s, 2 899s,1 745s, 1 468m, 1 452m 1 393m, 1 374m, and 1 319s cm^{-1}; *m/z* (EI) 182 $(M - CO)^+$, 99, and 55; (CI, NH_3) 228 $(M + NH_4^+)$, 211 $(M + H^+)$, 99, and 55.

Preparation of (1R,2R,4R,4′S)-4,4′,7,7-*Tetramethylbicyclo*-[2.2.1]*heptane*-2-*spiro*-2′-(1′,3′-*dioxolane*) (**5c**) *and its Diastereoisomer* (**5d**).—A stirred solution of D-camphor (1 g, 6.57 mmol), (*S*)-(+)-propane-1,2-diol (0.5 g, 6.5 mmol), and PTSA (0.1 g, 0.52 mmol) was heated at reflux in benzene (*ca.* 25 cm^3) for 18 h, as described for the preparation of compound (**4**). After the mixture had cooled, anhydrous sodium carbonate (0.5 g) was added and the suspension was filtered. Removal of solvent at reduced pressure (rotary evaporation) yielded an oil. Purification by column chromatography [Merck Kieselgel 60, Art 7734 (70–230 mesh), eluted with light petroleum (40–60 °C)-ethyl acetate (3:1, v/v)] gave a mixture of diastereoisomers (**5c**) and (**5d**). A crystalline product could not be obtained after attempted fractional crystallisation. The mixture was analysed by 220 MHz ^1H NMR spectroscopy without further purification.

Preparation of (1R,2S,4R,4′R)4,4′,7,7-*Tetramethylbicyclo*-[2.2.1]*heptane*-2-*spiro*-2′-(1′,3′-*dioxolane*) (**5a**) *and its Diastereoisomer* (**5b**).—These were prepared from D-camphor (1 g, 6.57 mmol) and (*R*)-(−)-propane-1,2-diol (0.5 g, 6.5 mmol) by using the same procedure described for dioxolanes (**5c**) and (**5d**). After work-up a crystalline product could not be obtained, and the mixture was analysed by 220 MHz ^1H NMR spectroscopy without further purification.

Preparation of (1S,2R,4R,4′S)-4,4′,7,7-*Tetramethylbicyclo*-[2.2.1]*heptane*-2-*spiro*-2′-(1′,3′-*dioxolan*)-3-*one* (**6a**).—A stirred solution of D-camphorquinone (1 g, 6.02 mmol), (*S*)-(+)-propane-1,2-diol (0.55 g, 6.02 mmol), and PTSA (0.1 g, 0.52 mmol) *was heated at reflux in benzene* (*ca.* 25 cm^3) for 24 h under nitrogen as described for the dioxolane (**4**). After the mixture had cooled, anhydrous sodium carbonate (0.5 g) was added, the suspension was filtered, and the solvent was removed at reduced pressure (rotary evaporation) to yield a yellow oil. Purification by gravity column chromatography [Merck Kieselgel 60, Art 7734 (70–230 mesh), eluted with (40–60) light petroleum–ethyl acetate (7:1, v/v)] gave an oil, which was crystallised from (40–60) light petroleum (−78 °C) to give the *title compound* (**6a**) as a crystalline solid (0.35 g, 26%), m.p. 35–37 °C; R_f 0.53 [silica gel; (40–60) light petroleum–ethyl acetate (7:1, v/v)]; $\delta_H(CDCl_3)$ 0.90 (s, 3 H, Me), 0.97 (s, 3 H, Me), 1.0 (s, 3 H, Me), 1.34 (d, 3 H, dioxolane Me), 1.55 (m, 1 H, 6-H_{exo}), 1.64 (m, 1 H, 5-H_{exo}), 1.77 (m, 1 H, 5-H_{endo}), 1.94 (d, 1 H, 1-H, *J* 5 Hz), 1.95 (m, 1 H, 6-H_{endo}), 3.77 (dd, *J* 8.1 Hz, 1 H, dioxolane C*H*H), 4.07 (dd, *J* 8.1 and 6.0 Hz, 1 H, dioxolane CH*H*), and 4.22 (m, 1 H, C*H*Me); $\delta_C(CDCl_3)$ 9.13 (CH_3), 18.14 (CH_3), 18.92 (dioxolane CH_3), 21.39 (CH_3), 21.35 (CH_2), 30.37 (CH_2), 43.33 (C-7), 52.09 (C-1), 57.92 (C-4), 71.08 (*C*HMe), 73.64 (dioxolane CH_2), and 107.24 (C-2), carbonyl resonance not recorded; ν_{max}(film) 2 960s, 2 930s, 1 760s, 1 458m, 1 397m, 1 375m, 1 318m, 1 160m, 1 130m, 1 040s, and 1 030s cm^{-1}; *m/z* (EI) 224 (M^+) and 196 $(M - CO)^+$; $[\alpha]_D^{20}$ +93.3° (*c* 1.5 in $CHCl_3$) (Found: C, 69.6; H, 9.0. $C_{13}H_{20}O_3$ requires C, 69.61; H, 8.98%). In another experiment, HPLC analysis (Spherisorb S5W column, 25 cm × 4.6 mm i.d., eluting with 0.25% THF in hexane at 2 cm^3 min^{-1}, UV detection at 325 nm) showed the presence of two dioxolanes in the ratio of 6:1. These were separated in one pass through a Spherisorb S5W preparative HPLC column (25 × 2 cm i.d.) eluting with 0.25% THF in hexane at 20 cm^3 min^{-1} to give dioxolanes (**6a**) and (**6b**) as colourless crystalline solids.

(**6a**): spectroscopic data as above.

(1S,2S,4R,4′S)-4,4′,7,7-*Tetramethylbicyclo*[2.2.1]*heptane*-2-*spiro*-2′-(1′,3′-*dioxolan*)-3-*one* (**6b**): m.p. 36.5–37.5 °C; δ_H(300 MHz; $CDCl_3$) 0.88 (s, 3 H, 10-Me), 0.96 (s, 3 H, 9-Me), 0.98 (s, 3 H, 8-Me), 1.25 (d, 3 H, dioxolane Me, *J* 6 Hz), 1.48–1.70 (m, 2 H, 5-H and 6-H_{exo}), 1.72–1.85 (m, 1 H, 5-H_{endo}), 1.91–2.05 (m, 1 H, 6-H_{endo}), 1.94 (d, 1 H, 1-H, *J* 5 Hz), 3.45 (dd, 1 H, dioxolane C*H*H*anti*, *J* 7.5 Hz), 4.30 (dd, 1 H, dioxolane CH*Hsyn*, *J* 7.5 Hz) and 4.50–4.63 (m, 1 H, dioxolane CH*syn*); ν_{max} 2 981s, 2 968s, 2 931s, 1 757s, 1 451m, 1 376m, 1 313m, 1 216m, 1 175m,

1 124m, 1 042s, 1 024s, and 992s cm^{-1}; *m/z* (CI, reagent CH_4); 225 (*M* + H), 167, 155, and 127.

Preparation of (1S,2R,4R,4′R)-4,4′,7,7-*Tetramethylbicyclo*[2.2.1]*heptane*-2-*spiro*-2′-(1′,3′-*dioxolan*)-3-*one* (**6c**) *and its isomers* (**6d**) *and* (**6e**).—These were prepared from D-camphorquinone (0.50 g, 3.0 mmol), PTSA (0.05 g, 2.8×10^{-4} mol), and (*R*)-(−)-propane-1,2-diol (0.32 g, 4.2 mmol) in the manner described for the preparation of (**6a**) and (**6b**). HPLC analysis of the initial product from chromatography showed the presence of four dioxolanes in the ratio of 6:47:40:7. These were separated in one pass on a Spherisorb S5W preparative HPLC column (25 × 2 cm i.d.) eluting with 0.25% THF in hexane at 20 cm^3 min^{-1}.

(1S,2S,4R,4′R)-4,4′,7,7-*Tetramethylbicyclo*[2.2.1]*heptane*-2-*spiro*-2′-(1′,3′-*dioxolan*)-3-*one* (**6d**): 47%, white crystalline solid, m.p. 44–46 °C; δ_H(300 MHz; $CDCl_3$) 0.90 (s, 3 H, 10-Me), 0.96 (s, 3 H, 9-Me), 0.99 (s, 3 H, 8-Me), 1.32 (d, 3 H, dioxolane Me, *J* 6 Hz), 1.48–1.69 (m, 2 H, 5-H and 6-H_{exo}), 1.70–1.83 (m, 1 H, 5-H_{endo}), 1.89–2.03 (m, 1 H, 6-H_{endo}), 1.92 (d, 1 H, 1-H, *J* 5 Hz), 3.86 (m, 1 H, dioxolane C*H*H_{anti}) and 4.08–4.22 (m, 2 H, dioxolane CH*Hsyn* and CH*anti*); ν_{max} 2 985s, 2 963s, 2 931s, 2 879s, 1 758s, 1 454m, 1 315s, 1 218s, 1 156s, 1 084m, 1 037s, 989s, and 942s cm^{-1}; *m/z* (CI, reagent CH_4) 225 (*M* + H), 196 and 167.

(1S,2R,4R,4′R)-4,4′,7,7-*Tetramethylbicyclo*[2.2.1]*heptane*-2-*spiro*-2′-(1′,3′-*dioxolan*)-3-*one* (**6c**): 40%,clear colourless liquid; δ_H(300 MHz, $CDCl_3$) 0.88 (s, 3 H, 10-Me), 0.95 (s, 3 H, 9-Me), 1.00 (s, 3 H, 8-Me), 1.26 (d, 3 H, dioxolane Me, *J* 6 Hz), 1.48–1.69 (m, 2 H, 5-H and 6-H_{exo}), 1.72–1.84 (m, 1 H, 5-H_{endo}), 1.92–2.04 (m, 1 H, 6-H_{endo}), 1.95 (d, 1 H, 1-H, *J* 6 Hz), 3.40 (dd, 1 H, dioxolane C*H*H*anti*, *J* 7.5 Hz), 4.19 (dd, 1 H, dioxolane CH*Hsym*, *J* 7.5 Hz), and 4.71 (m, 1 H, dioxolane CH*syn*); ν_{max} 2 964s, 2 931s, 2 876s, 1 757s, 1 479m, 1 455m, 1 395m, 1 374m, 1 171m, 1 135s, 1 084m, 1 039s, 1 022s, 992m, 956s, and 902m cm^{-1}; *m/z* (CI, reagent CH_4) 225 (*M* + H), 183, 167, 155, and 127.

(1R,2S,4S,4′R)-1,4′,7,7-*Tetramethylbicyclo*[2.2.1]*heptane*-2-*spiro*-2′-(1′,3′-*dioxolan*)-3-*one* (**6e**): 7%, clear colourless liquid; δ_H(300 MHz; $CDCl_3$) 0.89 (s, 3 H, 10-Me), 0.92 (s, 3 H, 9-Me), 1.00 (s, 3 H, 8-Me), 1.24 (d, 3 H, dioxolane Me, *J* 6 Hz), 1.48–1.63 (m, 2 H, 5-H and 6-H_{exo}), 1.82–1.96 (m, 1 H, 6-H_{endo}), 1.97–2.09 (m, 1 H, 5-H_{endo}), 2.15 (d, 1 H, 4-H, *J* 5 Hz), 3.38 (dd, 1 H, dioxolane C*H*H*anti*, *J* 7.5 Hz), 4.30 (dd, 1 H, dioxolane CH*Hsyn*, *J* 7.5 Hz) and 4.52 (m, 1 H, dioxolane CH*syn*); ν_{max} 2 964s, 2 933s, 2 877s, 1 759s, 1 477m, 1 455m, 1 395m, 1 374m, 1 147s, 1 108s, 1 035s, 1 013s, and 994m cm^{-1}; *m/z* (CI reagent CH_4) 225 (*M* + H), 183, 167, 155, and 127.

Preparation of (1S,2R,4R,4′R)-4′-*Chloromethyl*-4,7,7-*trimethylbicyclo*[2.2.1]*heptane*-2-*spiro*-2′-(1′,3′-*dioxolan*)-3-*one* (**7b**).—A stirred solution of D-camphorquinone (100 g, 0.6 mol), *rac*-3-chloropropane-1,2-diol (314 g, 2.86 mol), and PTSA (10 g, 0.052 mol) in benzene (1 750 cm^3) was heated at reflux for 18 h (Dean–Stark apparatus). After the mixture had cooled, anhydrous sodium sulphate (15 g) was added, the solid was filtered off, and the solvent was removed at reduced pressure (rotary evaporation) to yield a yellow liquid. This liquid was dissolved in water (1 000 cm^3) and the product was extracted with (40–60) light petroleum (3 × 500 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated to yield a yellow oil. Purification by gravity column chromatography [Merck Kieselgel 60, Art 7734 (70–230 mesh), eluted with (40–60) light petroleum–ethyl acetate (7:1, v/v)] gave a mixture of dioxolanes (**7a**)–(**7d**) from which compound (**7b**) crystallised. Repeated recrystallisation [(40–60) light petroleum] gave the *dioxolane* (**7b**) as a crystalline solid (14.6 g, 9.4%), m.p. 75.5–76.5 °C (starts to sublime at 61 °C); R_f 0.73 [silica gel; (40–60) light petroleum–ethyl acetate (7:1, v/v)]; δ_H(400 MHz; $CDCl_3$) 0.91 (s, 3 H, Me), 0.98 (s, 6 H, 2 × Me), 1.56 (m, 1 H, 6-H_{exo}), 1.66 (m, 1 H, 5-H_{exo}), 1.80 (m, 1 H, 6-H_{endo}), 1.94 (m, 1 H, 5-H_{endo}), 1.99 (d, 1 H, 1-H), 3.71 (m, 2 H, CH_2Cl), 4.03 (dd, *J* 6.67 and 8.6 Hz, 1 H, dioxolane C*H*H), 4.17 (dd, *J* 6.12 and 8.4 Hz, 1 H, dioxolane CH*H*), and 4.37 (m, 1 H, C*H*CH_2Cl); δ_C($CDCl_3$) 9.23 (CH_3), 18.97 (CH_3), 21.18 (CH_2), 21.38 (CH_3), 30.81 (CH_2), 43.48 (C-7), 44.13 (CH_2Cl), 52.06 (C-1), 58.17 (C-4), 68.83 (CH_2 dioxolane), 77.21 (*C*HCH_2Cl), 108.41 (C-2), and 216.31 (CO); ν_{max}(film) 2 960s, 2 920s, 2 870s, 1 745s, 1 464s, 1 398m, 1 374m, 1 320m, 1 222m, 1 130m, 1 030m, 736m, and 707w cm^{-1}; *m/z* (CI, NH_3) 278 and 276 (*M* + NH_4^+, 45.8%), 261 and 259 (M + H^+, 56.8), 232 and 230 [(*M* − CO)$^+$, 5.2], and 149 and 147 ($C_5H_5ClO_3^+$, 100) (ratios 1:3, respectively); $[\alpha]_D^{22}$ +90° (*c* 2.0 in CCl_4) (Found: C, 60.4; H, 7.45; Cl, 13.6. $C_{13}H_{19}ClO_3$ requires C, 60.34; H, 7.40; Cl, 13.70%).

HPLC Separation of Chloromethyldioxolanes (**7a–h**).—In another experiment, a stirred solution of D-camphorquinone (0.50 g, 3.0 mmol), PTSA (0.05 g, 2.8×10^{-4} mol), and *rac*-3-chloropropane-1,2-diol (1.2 cm^3, 1.59 g, 0.014 mol) in benzene (10 cm^3) was refluxed through a Dean and Stark apparatus for 18 h. After cooling, anhydrous sodium carbonate (0.15 g) was added. The solid was filtered off and washed with ethyl acetate (50 cm^3) and the combined filtrates were evaporated to yield a yellow oil. Water (10 cm^3) was added and the mixture was extracted with petroleum (b.p. 40–60 °C; 3 × 25 cm^3). The combined extracts were washed with saturated aqueous sodium hydrogen carbonate (10 cm^3), dried ($MgSO_4$), filtered, and evaporated to yield a yellow liquid. Purification by gravity column chromatography (silica gel, eluting with petroleum [b.p. 40–60 °C]–ethyl acetate [7:1 (v/v)]) gave a clear colourless liquid. HPLC analysis (Spherisorb S5W column, 25 cm × 4.6 mm i.d.; eluting with 0.25% t-butyl methyl ether (MTBE) in hexane at 1 cm^3 min^{-1}, UV detection at 325 nm) showed the presence of eight dioxolanes in the ratio of 23:24:10:5:14:14:3:7. These were separated on a Spherisorb S5W normal phase preparative HPLC column (25 × 2 cm i.d.) eluting with 0.25% t-butyl methyl ether in hexane at 17 cm^3 min^{-1}. The data for each compound is presented in order of their elution.

(1S,2S,4R,4′S)-4′-*Chloromethyl*-4,7,7-*trimethylbicyclo*[2.2.1]-*heptane*-2-*spiro*-2′-(1′,3′-*dioxolan*)-3-*one* (**7a**). Crystalline solid, m.p. 72–73 °C; δ_H(400 MHz; $CDCl_3$) 0.91 (s, 3 H, Me), 0.98 (s, 3 H, Me), 1.00 (s, 3 H, Me), 1.53 (m, 1 H, 6-H_{exo}), 1.66 (m, 1 H, 5-H_{exo}), 1.79 (m, 1 H, 6-H_{endo}), 1.95 (d, 1 H, 1-H), 1.96 (m, 1 H, 5-H_{endo}), 3.68 (d, 2 H, CH_2Cl), 4.19 (m, 2 H, dioxolane CH_2), and 4.29 (m, 1 H, C*H*CH_2Cl); ν_{max}(film) 2 960s, 2 920s, 2 870s, 1 754s, 1 464s, 1 398m, 1 374m, 1 320m, 1 222m, 1 130m, 736m, and 707w cm^{-1}; *m/z* (CI, NH_3) 278 and 276 (*M* + NH_4^+, 26.4%), 261 and 259 (*M* + H^+, 4.8), 232 and 230 [(*M* − CO)$^+$, 0.8], and 149 and 147 ($C_5H_5ClO_3^+$. 8.8) (ratio 1:3, respectively), 18,100%.

(**7b**): white crystalline solid, m.p. 77–79 °C, spectroscopic data as above.

(1R,2R,4S,4′R)-4′-*Chloromethyl*-1,7,7-*trimethylbicyclo*-[2.2.1]*heptane*-2-*spiro*-2′-(1′,3′-*dioxolan*)-3-*one* (**7h**): colourless oil; δ_H(300 MHz; $CDCl_3$) 0.88 (s, 3 H, 10-Me), 0.93 (s, 3 H, 9-Me), 1.01 (s, 3 H, 8-Me), 1.44–1.65 (m, 2 H, 5-H and 6-H_{exo}), 1.84–2.08 (m, 2 H, 5-H and 6-H_{endo}), 2.19 (d, 1 H, 4-H, *J* 5 Hz), 3.65 (d, 2 H, CH_2Cl), 4.12–4.23 (m, 2 H, dioxolane CH_2), and 4.23–4.32 (m, 1 H, dioxolane CH*anti*); ν_{max} 2 983m, 1 756s, 1 474m, 1 418m, 1 395m, 1 374m, 1 318m, 1 221m, 1 157s, 1 120s, 1 025s, 987s, 914m, and 822m cm^{-1}; *m/z* (CI, reagent CH_4); 259 and 261 (*M* + H, ratio 3:1), 223, 167, 161, 149, and 137.

(1R,2S,4S,4′S)-4′-*Chloromethyl*-1,7,7-*trimethylbicyclo*-[2.2.1]*heptane*-2-*spiro*-2′-(1′,3′-*dioxolan*)-3-*one* (**7g**): colourless

oil; δ_H(300 MHz; $CDCl_3$) 0.89 (s, 3 H, 10-Me), 0.93 (s, 3 H, 9-Me), 0.97 (s, 3 H, 8-Me), 1.46–1.63 (m, 2 H, 5-H and 6-H_{exo}), 1.84–2.08 (m, 2 H, 5-M and 6-H_{endo}), 2.16 (d, 1 H, 4-H, *J* 5 Hz), 3.60–3.76 (m, 2 H, CH_2Cl), 3.97 (dd, 1 H, dioxolane C*H*H*anti*, *J* 7.5 Hz), 4.17 (dd, 1 H, dioxolane CH*Hsyn*, *J* 7.5 Hz) and 4.27–4.38 (m, 1 H, dioxolane CH*anti*); ν_{max} 2 983m, 1 756s, 1 473m, 1 454m, 1 394m, 1 370m, 1 194m, 1 114s, 1 032s, and 1 018s cm^{-1}; *m/z* (CI, reagent CH_4) 259 and 261 (*M* + H, ratio 3:1), 223, 167, 161, and 147.

(1S,2R,4R,4'S)-4'-*Chloromethyl*-4,7,7-*trimethylbicyclo*-[2.2.1]*heptane*-2-*spiro*-2'-(1',3'-*dioxolan*)-3-*one* (**7c**). Crystalline solid, m.p. 52–53 °C; δ_H(400 MHz; $CDCl_3$) 0.90 (s, 3 H, Me), 0.97 (s, 3 H, Me), 0.99 (s, 3 H, Me), 1.56 (m, 1 H, 6-H_{exo}), 1.65 (m, 1 H, 5-H_{exo}), 1.81 (m, 1 H, 6-H_{endo}), 1.97 (m, 1 H, 5-H_{endo}), 1.98 (d, 1 H, 1 H), 3.46 (dd, *J* 7.56 and 10.85 Hz, 1 H, C*H*HCl), 3.57 (dd, *J* 4.48 and 10.85 Hz, 1 H, CH*H*Cl), 3.90 (dd, *J* 3.92 and 8.2 Hz, 1 H, dioxolane C*H*H), 4.35 (dd, *J* 6.96 and 8.2 Hz, 1 H, dioxolane CH*H*), and 4.70 (m, 1 H, C*H*CH_2Cl); δ_C($CDCl_3$) 9.0 (CH_3), 18.8 (CH_2), 21.2 (CH_3), 21.3 (CH_3), 30.7 (CH_2), 43.5 (C-7), 44.2 (CH_2Cl), 51.8 (C-1), 58.1 (C-4), 67.25 (dioxolane CH_2), 108 (C-2), and 216 (CO); dioxolane CH under $CDCl_3$; ν_{max}(film) 2 992s, 2 960s, 2 923s, 2 878s, 1 754s, 1 482s, 1 456s, 1 443s, 1 397m, 1 372m, 1 320m, 1 222m, 1 138m, and 707w cm^{-1}; *m/z* (CI, NH_3) 278 and 276 (*M* + NH_4^+, 63.2%), 261 and 259 (*M* + H^+, 30.8), 232 and 230 [(*M* − CO)$^+$, 15.4], and 149 and 147 ($C_5H_5ClO_3^+$, 76%) (ratio 1:3, respectively), 18, 100% $[\alpha]_D^{28}$ +48° (*c* 1.6 in $CHCl_3$).

(1S,2S,4R,4'R)-4'-*Chloromethyl*-4,7,7-*trimethylbicyclo*[2.2.1]-*heptane*-2-*spiro*-2'-(1',3'-*dioxolan*)-3-*one* (**7d**). Crystalline solid, m.p. 53–54 °C; δ_H(400 MHz; $CDCl_3$) 0.91 (s, 3 H, Me), 0.98 (s, 3 H, Me), 1.07 (s, 3 H, Me), 1.56 (m, 1 H, 6-H_{exo}), 1.66 (m, 1 H, 5-H_{exo}), 1.81 (m, 1 H, 6-H_{endo}), 1.98 (d, 1 H, 1-H), 1.99 (m, 1 H, 5-H_{endo}), 3.46 (dd, *J* 7.2 and 10.8 Hz, 1 H, C*H*HCl), 3.57 (dd, *J* 4.56 and 10.8 Hz, 1 H, CH*H*Cl), 3.97 (dd, *J* 4.0 and 8.2 Hz, 1 H, dioxolane C*H*H), 4.49 (dd, *J* 6.6 and 8.2 Hz, 1 H, dioxolane CH*H*), and 4.58 (m, 1 H, C*H*CH_2Cl); δ_C($CDCl_3$) 8.97 (CH_3), 18.84 (CH_2), 21.24 (CH_3), 21.40 (CH_3), 30.81 (CH_2), 43.52 (C-7), 44.25 (CH_2Cl), 51.91 (C-1), 58.2 (C-4), 69.22 (dioxolane CH_2), 74.67 (*C*HCH_2Cl), 108.1 (C-2), and 216 (CO); ν_{max}(film) 2 992s, 2 960s, 2 924s, 2 878s, 1 755s, 1 482s, 1 456s, 1 443s, 1 398m, 1 374m, 1 321m, 1 222m, 1 138m, and 707m cm^{-1}; *m/z* (CI, NH_3) 278 and 276 (*M* + NH_4^+, 35%), 261 and 259 (*M* + H^+, 12), 232 and 230 [(*M* − CO)$^+$, 5.8], and 149 and 147 ($C_5H_5ClO_3^+$, 58.8%) (ratio 1:3, respectively); 18, 100%; $[\alpha]_D^{29}$ +69° (*c* 1.09 in $CHCl_3$).

(1R,2S,4S,4'R)-4'-*Chloromethyl*-1,7,7-*trimethylbicyclo*-[2.2.1]*heptane*-2-*spiro*-2'-(1',3'-*dioxolan*)-3-*one* (**7f**): colourless oil; δ_H(300 MHz; $CDCl_3$) 0.89 (s, 3 H, 10-Me), 0.93 (s, 3 H, 9-Me), 0.97 (s, 3 H, 8-Me), 1.47–1.68 (m, 2 H, 5-H and 6-H_{exo}), 1.84–2.08 (m, 2 H, 5-H and 6-H_{endo}), 2.15 (d, 1 H, 4-H, *J* 5 Hz), 3.42 (dd, 1 H, one of CH_2Cl, *J* 8 and 10 Hz), 3.54 (dd, 1 H, one of CH_2Cl, *J* 8 and 10 Hz), 3.87 (dd, 1 H, dioxolane C*H*H*anti*, *J* 3 and 8 Hz), 4.31 (dd, 1 H, dioxolane CH*Hsyn*, *J* 7 Hz) and 4.65 (m, 1 H, dioxolane CH*syn*); ν_{max} 2 961m, 1 756s, 1 473m, 1 395m, 1 374m, 1 137m, 1 115s, 1 060m, 1 018s, 989s, 963m, and 904m cm^{-1}; *m/z* (CI, reagent CH_4) 259 and 261 (*M* + H, ratio 3:1), 223, 167, 161, 147, and 137.

(1R,2R,4S,4'S)-4'-*Chloromethyl*-1,7,7-*trimethylbicyclo*-[2.2.1]*heptane*-2-*spiro*-2'-(1',3'-*dioxolan*)-3-*one* (**7e**): colourless oil; δ_H(300 MHz; $CDCl_3$) 0.91 (s, 3 H, 10-Me), 0.95 (s, 3 H, 9-Me), 1.01 (s, 3 H, 8-Me), 1.47–1.64 (m, 2 H, 5-H and 6-H_{exo}), 1.84–2.11 (m, 2 H, 5-H and 6-H_{endo}), 2.16 (d, 1 H, 4-H, *J* 5 Hz), 3.16 (dd, 1 H, one of CH_2Cl, *J* 7 and 10 Hz), 3.56 (dd, 1 H, one of CH_2Cl, *J* 7 and 10 Hz), 3.91 (dd, 1 H, dioxolane C*H*H*anti*, *J* 5 and 7 Hz), and 4.46–4.59 (m, 2 H, dioxolane CH*H* and CH*syn*); ν_{max} 2 961m, 1 756s, 1 475m, 1 395m, 1 374m, 1 156m, 1 118s, 1 076s, 1 054m, 1 002m, and 906m cm^{-1}; *m/z* (CI, reagent CH_4) 259 and 261 (*M* + H, ratio 3:1), 230, 223, 167, and 161.

Preparation of (1R,2S,4S,4'S)-4'-*Chloromethyl*-4,7,7-*trimethylbicyclo*[2.2.1]*heptane*-2-*spiro*-2-(1',3'-*dioxolan*)-3-*one* (**9**).—This was prepared from L-camphorquinone (1.926 g, 1.1 × 10^{-2} mol) and *rac*-3-chloropropane-1,2-diol (12.76 g, 0.116 mol) as described for the dioxolane (**6a**). Recrystallisation from light petroleum gave the title compound as a crystalline solid (0.32 g, 11.4%), m.p. 74–76 °C; $[\alpha]_D^{20}$ −71° (*C* 1.5 in $CHCl_3$). Spectral properties were identical with those of the dioxolane (**7b**).

Preparation of (1S,2R,4R,4'R)-4'-*t-Butyl*-4,7,7-*trimethylbicyclo*[2.2.1]*heptane*-2-*spiro*-2'-(1',3'-*dioxolane*)-3-*one* (**8a**) *and its Diastereoisomers* (**8b**, **c** *and* **d**).—A stirred solution of D-camphorquinone (0.5 g, 3.01 mmol), *rac*-3,3-dimethylbutane-1,2-diol (3.0 g, 2.3 × 10^{-2} mol), and PTSA (0.05 g, 0.26 mmol) was heated (18 h) at reflux in benzene (*ca.* 30 cm^3) as described for the dioxolane (**6a**). After work-up the resulting yellow oil was purified by gravity column chromatography [Merck Kieselgel 60, Art 7734 (70–230 mesh) eluted with (40–60) light petroleum–ethyl acetate (7:1, v/v)] to give an oil (0.686 g, 85.7%) which did not crystallise. HPLC analysis (Spherisorb S5W column, 25 cm × 4.6 mm i.d.; eluting with 0.25% t-butyl methyl ether in hexane at 1 cm^3 min^{-1}, UV detection at 325 nm) showed the presence of seven dioxolanes in the ratio of 4:15:5:60:3:9:4. An analytical sample of the *major dioxolane* was obtained by HPLC [Whatman Partisil M20: 10/50 (50 cm × 22 mm i.d.), eluted with 1% ethyl acetate in hexane (v/v), flow rate 7.5 cm^3 min^{-1}]: b.p. (Kugelröhr distillation) 75–79 °C/0.2 mmHg; R_f 0.65 [silica gel; (40–60) light petroleum–ethyl acetate (7:1, v/v)]; δ_H(300 MHz; $CDCl_3$) 0.91 (s, 3 H, Me), 0.93 (s, 9 H, But), 0.97 (s, 3 H, Me), 1.00 (s, 3 H, Me), 1.52–1.98 (m, 4 H, 5- and 6-Hz), 1.94 (d, 1 H, 1-H), 3.73 (dd, *J* 5.7 and 9.4 Hz, dioxolane C*H*H), and 3.93 (m, 2 H, C*H*Bu^t and dioxolane CH*H*); ν_{max}(film) 2 963s, 2 910s, 2 875s, 1 764s, 1 482m, 1 398m, 1 369m, 1 320m, 1 225m, 1 127m, 1 026s, and 947m cm^{-1}; *m/z* 266 (*M*$^+$), 251 (*M* + CH_3), 238 (*M* − CO)$^+$, 223 (*M* − CO − CH_3)$^+$, and 155; $[\alpha]_D^{22}$ +30.4° (*c* 1.56 in CCl_4); *m/z* (EI) 266.1885 (*M*$^+$). ($C_{16}H_{26}O_3$ requires *M*, 266.1882).

Preparation of (1S,2R,3S,4R,4'S)-4,4',7,7-*Tetramethylbicyclo*-[2.2.1]*heptane*-2-*spiro*-2'-(1',3'-*dioxolan*)-3-*ol* (**12a**).—To a stirred solution of the dioxolane (**7b**) (0.2 g, 0.77 mmol) in dry THF (5 cm^3) under nitrogen was added lithium tri-s-butylborohydride (L-Selectride) (3.08 mmol; 3.08 cm^3 of a 1M solution in THF) and the reaction mixture was heated to 40 °C. TLC analysis [silica gel; (40–60) light petroleum–ethyl acetate (7:1, v/v)] indicated complete reaction after 14 h. Water (10 cm^3) was carefully added and the product was extracted into (40–60) light petroleum (3 × 10 cm^3). The extracts were combined, washed with water (2 × 10 cm^3), dried ($MgSO_4$), and evaporated at reduced pressure (rotary evaporation) to give an oil, which was purified by gravity column chromatography [Merck Kieselgel 60, Art 9385 (230–400 mesh) eluted with (40–60) light petroleum–ethyl acetate (7:1, v/v)] to give the *alcohol* (**12a**) as an oil (140 mg, 83%), b.p. 36–38 °C/0.1 mmHg; R_f 0.41; δ_H(300 MHz; $CDCl_3$) 0.83 (s, 3 H, Me), 0.91 (s, 3 H, Me), 1.07 (s, 3 H, Me) 1.18 (m, 1 H, 5-H_{endo}), 1.32 (d, 3-H, dioxolane Me), 1.45–1.80 (m, 4 H, 6-H_2, 5-H_{exo}, and 1-H), 2.54 (br s, 1 H, CHO*H*), 3.24 (s, 1 H, C*H*OH), 3.33 (dd, *J* 8.17 Hz, 1 H, dioxolane C*H*H), 3.97 (dd, *J* 5.5 and 8.17 Hz, 1 H, dioxolane CH*H*), and 4.24 (m, 1 H, C*H*Me); ν_{max}(film) 3 530br, 2 930s, 2870s, 1 478m, 1 454m, 1 393m, 1 371m, 1 309m, 1 226m, 1 094s, and 994m cm^{-1}; *m/z* (EI) 226 (*M*$^+$), 211 (*M* − CH_3)$^+$. 155, and 141; $[\alpha]_D^{22}$ +26.4° (*c* 1.45 in CCl_4); *m/z* (EI) 226.1574 (*M*$^+$) ($C_{13}H_{22}O_3$ requires *M*, 226.1569).

Oxidation of (1S,2R,3S,4R,4'S)-4,4',7,7-*Tetramethylbicyclo*[2.2.1]*heptane*-2-*spiro*-2'-(1',3'-*dioxolan*)-3-*ol* (**12a**).—To a solution of the dioxolane (**12a**) (20 mg, 8.85×10^{-2} mmol) in DMF (0.5 cm^3) was added PDC (0.33 g, 0.885 mmol) and the reaction mixture was stirred under nitrogen at room temperature. TLC analysis [silica gel; (40–60) light petroleum–ethyl acetate (7:1, v/v)] showed the reaction to be complete after 20 h. The reaction mixture was filtered through a short column of magnesium sulphate (*ca.* 1 g) and the column was washed with (40–60) light petroleum (10 cm^3). The eluate was washed with water (4×5 cm^3), dried ($MgSO_4$), and evaporated at reduced pressure to leave an oil (16 mg, 81%) which crystallised on storage, m.p. 35–36 °C [recrystallisation from (40–60) light petroleum], R_f 0.57; all other physical properties were identified with those of the dioxolane (**6a**).

Reduction of (1S,2R,4R,4'R)-4'-*Chloromethyl*-4,7,7-*trimethylbicyclo*[2.2.1]*heptane*-2-*spiro*-2'-(1',3'-*dioxolan*)-3-*one* (**7b**) *with Diborane*.—To a stirred solution of the dioxolane (**7b**), (0.2 g, 0.774 mmol) in THF (2 cm^3) under nitrogen at −10 °C was added diborane (3.7 mmol; 3.7 cm^3 of a 1M solution in THF) and the reaction mixture was warmed to 40 °C. TLC analysis [silica gel; (40–60) light petroleum–ethyl acetate (7:1, v/v)] indicated the reaction to be complete after 96 h. Water (0.5 cm^3) was slowly added and the organoboranes were hydrolysed at 30–50 °C by addition of 3M-sodium hydroxide (0.5 cm^3) followed by dropwise addition of 30% hydrogen peroxide (0.4 cm^3). The product was extracted into (40–60) light petroleum (20 cm^3) and the extract was washed with water (2×5 cm^3), dried ($MgSO_4$), and evaporated at reduced pressure (rotary evaporation) to yield an oil (0.18 g, 87%), R_f 0.45. ^1H NMR analysis showed the product to be a mixture of C-3 *exo*- and *endo*-alcohol (**10a**) and (**10b**), respectively, in the ratio 14:3 (82% *exo*), respectively; δ_H($CDCl_3$; *exo*-alcohol) 0.83 (s, 3 H, Me), 0.91 (s, 3 H, Me), 1.09 (s, 3 H, Me), 1.18 (m, 1 H, 5-H_{endo}), 1.48–1.75 (m, 4 H, 6-H_2, 5-H_{exo}, and 1 H), 2.38 (br s, 1 H, CHO*H*), 3.33 (s, 1 H, C*H*OH), 3.63 (m, 2 H, CH_2Cl), 3.77 (dd, *J* 5.7 and 8.73 Hz, 1 H, dioxolane C*H*H), 3.98 (dd, *J* 5.9 and 8.73 Hz, 1 H, dioxolane CH*H*), and 4.34 (m, 1 H, C*H*CH_2Cl); the *endo*-alcohol was identified by resonances at δ_H 0.87 (s, 3 H, Me), 0.88 (s, 3 H, Me), 1.03 (s, 3 H, Me), 3.48 (dd, *J* 8.1 and 10.8 Hz, 1 H, C*H*HCl), 3.86 (dd, *J* 5.1 and 8.3 Hz, 1 H, dioxolane C*H*H), and 4.31 (m, 1 H, C*H*CH_2Cl); *m/z* (EI) 262 and 260 (M^+) (ratio 1:3, respectively).

Reduction of (1S,2R,4R,4'R)-4'-*chloromethyl*-4,7,7-*trimethylbicyclo*[2.2.1]*heptane*-2-*spiro*-2'-(1',3'-*dioxolan*)-3-*one* (**7b**) *with Sodium Borohydride*.—To a stirred solution of the dioxolane (**7b**) (0.5 g, 1.9 mmol) in ethanol (10 cm^3) was added sodium borohydride (8.66×10^{-2} g, 2.34 mmol) during *ca.* 10 min and the reaction mixture was heated to 40 °C. Monitoring [TLC; light petroleum–ethyl acetate (7:1, v/v)] showed the reaction to be complete after 4 h. Water (2 cm^3) was added and volatiles were removed at reduced pressure. The resulting oil was dissolved in diethyl ether (10 cm^3), and the solution was washed with water (3×5 cm^3), dried (Na_2SO_4), and evaporated to give an oil (4.42 g, 89.4%), R_f 0.43. ^1H NMR analysis showed the product to be a mixture of C-3 *exo*- and *endo*-alcohol (**10a**) and (**10b**), respectively, in the ratio 3:1 (75% *exo*), respectively.

Reduction of (1S,2R,4R,4'R)-4'-*Chloromethyl*-4,7,7-*trimethylbicyclo*[2.2.1]*heptane*-2-*spiro*-2'-(1',3'-*dioxolan*)-3-*one* (**7b**) *with Lithium Tri-t-butoxyaluminium Hydride*.—A solution of t-butyl alcohol (2.15 g, 2.90×10^{-2} mol) in THF (0.5 cm^3) was added dropwise during *ca.* 30 min to a stirred suspension of lithium aluminium hydride (0.368 g, 9.68 mmol) in THF (5 cm^3) at −10 °C under nitrogen. The reaction mixture was allowed to warm to room temperature and after 2 h a solution of the dioxolane (**7b**) (0.5 g, 1.93 mmol) in THF (2 cm^3) was added during 2 min. TLC analysis [silica gel; (40–60) light petroleum–ethyl acetate (7:1, v/v)] indicated complete reaction after 20 h. Water (3 cm^3) was slowly added and the white precipitate (LiOH) was filtered off (Celite) and washed with (40–60) light petroleum (50 cm^3). The filtrate was evaporated at reduced pressure (rotary evaporation) to give a crude oily product, which was redissolved in (40–60) light petroleum (15 cm^3), and the solution was washed with water (2×3 cm^3), dried ($MgSO_4$), then filtered, and evaporated at reduced pressure to give compound (**10a**) as an oil (0.47 g, 93%); R_f 0.45; δ_H(300 MHz; $CDCl_3$) 0.83 (s, 3 H, Me), 0.91 (s, 3 H, Me), 1.09 (s, 3 H, Me), 1.18 (m, 1 H, 5-H_{endo}), 1.48–1.75 (m, 3 H, 6-H_2 and 5-H_{exo}), 1.74 (d, 1 H, 1-H), 2.54 (br s, 1 H, CHO*H*), 3.33 (s, 1 H, C*H*OH), 3.63 (m, 2 H, CH_2Cl), 3.77 (dd, *J* 5.7 and 8.73 Hz, 1 H, dioxolane C*H*H), 3.98 (dd, *J* 5.9 and 8.73 Hz, 1 H, dioxolane CH*H*), and 4.34 (m, 1 H, C*H*CH_2Cl); ν_{max}(film) 3 540br, 2 980s, 2 892s, 1 479m, 1 454m, 1 393m, 1 372m, 1 308m, 1 094s, 993s, and 742w cm^{-1}; *m/z* (EI) 260 and 262 (M^+) (ratio 3:1, respectively), 245 and 247 ($M - CH_3$)$^+$ (ratio 3:1, respectively), 189 and 191 (ratio 3:1, respectively), and 175 and 177 (ratio 3:1, respectively); $[\alpha]_D^{18}$ +36° (*c* 2.13 in CCl_4); *m/z* (EI) 260.1189 (M^+) ($C_{13}H_{21}ClO_3$ requires *M*, 260.1179).

Reduction of (1S,2R,4R,4'R)-4'-*Chloromethyl*-4,7,7-*trimethylbicyclo*[2.2.1]*heptane*-2-*spiro*-2'-(1',3'-*dioxolan*)-3-*one* (**7b**) *with Lithium Trimethoxyaluminium Hydride*,— Methanol (0.186 g, 5.8 mmol) was added during *ca.* 30 min to a stirred suspension of lithium aluminium hydride (7.35×10^{-2} g, 1.93 mmol) in THF (0.5 cm^3) at −10 °C under nitrogen. The reaction mixture was allowed to warm to 0 °C and, after 2 h, a solution of the dioxolane (**7b**) (0.1 g, 0.387 mmol) in THF (0.5 cm^3) was added dropwise. The reaction mixture was allowed to warm to room temperature and monitored by TLC [silica gel; (40–60) light petroleum–ethyl acetate (7:1, v/v)]. After 20 h, water (0.2 cm^3) was slowly added and the white precipitate was filtered off (Celite) and washed with (40–60) light petroleum (15 cm^3). The filtrate was washed with water (3×5 cm^3) and the light petroleum layer was dried ($MgSO_4$), filtered, and evaporated at reduced pressure (rotary evaporation) to give an oil (74.2 mg), R_f 0.43. ^1H NMR analysis showed the product to be a mixture of the dioxolane (**12a**) and the dioxolane (**10a**) in the ratio 5:2, respectively.

Preparation of (1R,2S,5R,6S,9S)-5,13,13-*Trimethyl*-7,11,12-*trioxatricyclo*[$7.2.1.1^{2,5}.0^{1,6}$]*tridecane* (**11**).—To a stirred solution of sodium hydride (0.11 g, 4.66 mmol) in THF (4 cm^3) under nitrogen was added a solution of dioxolane (**10a**) (59.7 mg, 0.229 mmol) in THF (1 cm^3) and the reaction mixture was heated to 55–60 °C. Aliquots were removed at intervals and analysis by TLC [silica gel; (40–60) light petroleum–ethyl acetate (7:1, v/v)] showed the reaction to be complete after 24 h. Water (15 cm^3) was slowly added and the product was extracted into (40–60) light petroleum (3×10 cm^3). The extracts were combined, washed with water (2×5 cm^3), dried ($MgSO_4$), filtered, and evaporated at reduced pressure (rotary evaporation) to give *tricyclo compound* (**11**) as an oil (41.8 mg, 81.3%), b.p. 50–55 °C/0.2 mmHg (Kugelröhr distillation); R_f 0.31; δ_H(300 MHz; $CDCl_3$) 0.87 (s, 3 H, Me), 0.88 (s, 3 H, Me), 1.24 (m, 1 H, 4-H_{endo}), 1.28 (s, 3 H, CH_3), 1.54–1.83 (m, 3 H, 3-H_2 and 4-H_{exo}), 1.87 (d, 1 H, 2-H), 2.87 (s, 1 H, 6-H_{endo}), 3.28 (dd, *J* 1.26 and 10.22 Hz, 1 H, OC*H*H_{endo}), 3.54 (dd, *J* 1.54 and 7.83 Hz, 1 H, OC*H*H_{endo}), 3.86 (ddd, *J* 1.00, 5.97, and 7.83 Hz, 1 H, OCHH_{exo}), 4.20 (ddd, *J* 1.00, 7.23, and 10.2 Hz, 1 H, OCHH_{exo}), and 4.50 (ddt, 1 H, 9-H); ν_{max}(film) 2 978s, 2 896s, 1 479m, 1 459m, 1 394m, 1 374m, 1 338m, 1 228w, 1 204m, 1 140s, 1 124s, 1 099m, 1 086m, 923m, and 857m cm^{-1}; *m/z* (EI) 224 (M^+), 209 ($M - CH_3$)$^+$, 193 ($M - CO$)$^+$, 181 ($M - CH_3 - CO$)$^+$, 141,

and 95; $[\alpha]_D^{22}$ −24° (*c* 1.99 in CCl_4); *m/z* (EI) 224.1414 (M^+) ($C_{13}H_{20}O_3$ requires *M*, 224.1412) (Found: C, 69.7; H, 8.8. $C_{13}H_{20}O_3$ requires C, 69.61; H, 8.98%).

Preparation of rac-2-*Acetoxy*-1-*bromo*-3-*chloropropane*.—To stirred 3-chloropropane-1,2-diol (11.0 g, 0.1 mol) at 0 °C was added 45% (w/v) hydrogen bromide in acetic acid (HBA) (106.5 g, 0.45 mol) during 5 min. After being stirred at room temperature for 1.5 h the solution was quickly added to ice-cooled water (150 cm^3) and was immediately neutralised with solid sodium carbonate. The neutral solution was extracted with diethyl ether (3 × 150 cm^3), and the extracts were combined, dried ($MgSO_4$), and evaporated at reduced pressure (rotary evaporation) to give a yellow oil (20.81 g, 97.4%). Fractional distillation gave the desired product as an oil (19.66 g, 92%), b.p. 90–92 °C/13 mmHg; $\delta_H(CDCl_3)$ 2.12 (s, 3 H, OAc), 3.60 (d, 2 H, CH_2Br), 3.76 (d, 2 H, CH_2Cl), and 5.15 (m, 1 H, C*H*OAc); ν_{max}(film) 3 020w, 2 965w, 1 748s, 1 430m, 1 372s, 1 230s, and 1 030s cm^{-1} (Found: C, 28.0; H, 3.9. $C_5H_8BrClO_2$ requires C, 27.9; H, 3.8%).

Preparation of (R)-(−)-3-*Chloropropane*-1,2-*diol*.—The dioxolane (**7b**) (0.5 g, 1.9 mmol) was reduced with sodium borohydride (0.14 g, 3.8 mmol) under the conditions previously described. To the product diols was added 2M-HCl (3 cm^3), followed by methanol until the reaction mixture was homogeneous. After the mixture had been refluxed for 3 h, volatiles were evaporated off and water (10 cm^3) was added. The aqueous solution was washed with (40–60) light petroleum (3 × 10 cm^3) and evaporated to leave a pale yellow oil, which was dissolved in dichloromethane; the solution was dried ($MgSO_4$), filtered, and evaporated at reduced pressure (rotary evaporation) to give the crude product. Kugelröhr distillation gave (*R*)-(−)-3-chloropropane-1,2-diol (115 mg, 55%) as an oil, b.p. 74–76 °C/15 mmHg; $\delta_H(CDCl_3)$ 3.0 (brs, 2 H, 2 × OH), 3.62 (m, 2 H, CH_2Cl), 3.73 (m, 2 H, CH_2OH), and 3.94 (m, 1 H, C*H*OH); $[\alpha]_D^{19}$ −7.4° (*c* 1.0 in water) {lit.,[12] $[\alpha]_D^{20}$ +7.3° (*c* 1.0 in water) for (*S*)-isomer}.

Preparation of (R)-(*Chloromethyl*)*oxirane* (**1a**).—HBA (13.02 g, 5.5 × 10^{-2} mol) was added to the stirred dioxolane (**7b**) (3 g, 1.16 × 10^{-2} mol) and the mixture was heated to 65 °C for 5 h. After cooling, the solution was quickly added to ice-cooled water (100 cm^3), immediately neutralised with solid sodium carbonate, and extracted with diethyl ether (3 × 30 cm^3). The extracts were combined, dried ($MgSO_4$), and evaporated at reduced pressure (rotary evaporation) to yield a yellow oil. ^1H NMR analysis showed the presence of 2-acetoxy-1-bromo-3-chloropropane: $\delta_H(CDCl_3)$ 2.13 (s, 3 H, OAc), 3.60 (d, 2 H, CH_2Br), 3.77 (d, 2 H, CH_2Cl), and 5.15 (m, 1 H, C*H*OAc).

The yellow oil (containing *ca.* 2.37 g, 1.1 × 10^{-2} mol of product) was vigorously stirred in dry ethane-1,2-diol (5 cm^3) and 1.2M-sodium ethane-1,2-diolate in ethane-1,2-diol (9.17 cm^3, 1.1 × 10^{-2} mol) was added dropwise during 15 min. The reaction mixture was stirred for 15 min after which the pressure was reduced to 0.2 mmHg and the product was distilled into an efficiently cooled receiver (−196 °C). After 30 min a further aliquot of 1.2M-sodium ethane-1,2-diolate in ethane-1,2-diol (2.29 cm^3, 2.9 mmol) was added and the reaction was allowed to continue for a further 30 min. Kugelröhr distillation of the crude product gave (*R*)-(chloromethyl)oxirane (**1a**) as a liquid [0.594 g, 58% from dioxolane (**7b**)]; b.p. 115–116 °C; $\delta_H(CDCl_3)$ 2.7 (dd, 1 H, oxirane C*H*H), 2.90 (dd, 1 H, oxirane CHH), 3.25 (m, 1 H, CH), and 3.59 (d, 2 H, CH_2Cl); $[\alpha]_D^{16}$ −33° (*c* 1.5 in MeOH) {lit.,[2] $[\alpha]_D^{20}$ +33° (*c* 1.13 in MeOH) for (*S*)-isomer}.

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